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RESPONSE UNDER C.F.R. § 1.116
EXPEDITED PROCEDURE
ART UNIT 1655

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Maura C. Cannon, Francis C. Cannon, Gabriel J. McCool, Henry E. Valentin, and Kenneth J. Gruys

Serial No.: 09/479,040 Art Unit: 1634

Filed: January 7, 2000 Examiner: A. Chakrabarti

For: *"POLYHYDROXYALKANOATE BIOSYNTHESIS ASSOCIATED PROTEINS AND CODING REGION IN BACILLUS MEGATERIUM"*

Do not Enter
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11/5/02

BOX AF
Assistant Commissioner for Patents
Washington, D.C. 20231

RESPONSE TO OFFICE ACTION

Sir:

The following remarks are in response to the Office Action mailed on July 26, 2002.

It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-1868.

Remarks

Claims 1, 3-6, 9, 11-14, 24 and 25 are pending.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1, 3-6, 9, 11-14, and 24-25 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention.

The present invention is directed to isolated or purified nucleic acid segments predicated on their ability to hybridize under stringent conditions to already isolated nucleic acid targets. For example, an isolated nucleic acid sequence comprising a sequence encoding a 3-keto-acyl-CoA reductase protein, wherein the sequence hybridizes to SEQ ID NO:8 or the complement thereof, and encodes a protein at least about 80% identical to SEQ ID NO:9, and has 3-keto-acyl-CoA reductase activity higher for D-isomers of C6 carbon chains than for C4 carbon chains. As will be further discussed below, the functionality of the protein encoded by the nucleic acid, in combination with the defined structural features dictated by hybridization to a target sequence, clearly convey that the applicants are in possession of the claimed compositions.

The Legal Standard

The first paragraph of 35 U.S.C. § 112 sets forth the written description requirement for patents as follows:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make

and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

The standard regarding what is or is not supported by the specification has been clearly articulated as "requiring the specification to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, the inventor was in possession of the invention", i.e., whatever is now claimed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111, 1117 (Fed . Cir. 1991). Compliance with the written description requirement is essentially a fact-based inquiry that will "necessarily vary depending on the nature of the invention claimed." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) (citing *In re DiLeone*, 436 F.2d 1404, 1405 (CCPA 1971)). Satisfaction of the written description requirement is determined on a case-by-case basis.

The inquiry into whether or not there is an adequate written description is not performed in a vacuum. "Knowledge of one skilled in the art is relevant to meeting [the written description] requirement." *Enzo Biochem, Inc. v. Gen-Probe*, Docket No. 01-1230 (Fed. Cir. Apr. 2, 2002) (slip op.). This fact has implications not only for validity challenges, but also for patent prosecution. *See In re Alton*, 76 F.3d 1168, 1174-75 (Fed. Cir. 1996).

Application Meets Legal Requirements for Written Description

In its Guidelines, the USPTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled *with a known or disclosed*

correlation between function and structure, or some combination of such characteristics." Guidelines, 66 Fed. Reg. at 1106 (emphasis added). The Applicants maintain that the inquiry into an adequate written description is not performed in a vacuum. Again, this is based upon Enzo Biochem, Inc. v. Gen-Probe, Docket No. 01-1230 (Fed. Cir. April 2, 2002) (slip op.), wherein "knowledge of one skilled in the art is relevant to meeting [the written description] requirement". The Examiner has rejected this notion, asserting that the specification lacks "alternative methods" (see page 7 of the Office Action mailed on July 26, 2002). The Examiner appears to be completely misguided in his understanding of the claimed compositions and how knowledge of one skilled in the art is applied to the pending claims. The art has established a strong correlation between nucleic acid structure and hybridization. The applicants are unsure why the Examiner requires one to provide "alternative methods" when one of ordinary skill in the art would realize that any known method that relies upon hybridization would sufficiently delineate between those claimed sequences that bind to the target sequence (SEQ ID NO:8 and SEQ ID NO:10) and those that do not bind. The claimed compositions are required to 1) be at least about 80% *identical* to SEQ ID NO:8, ***and*** 2) hybridize under stringent conditions to SEQ ID NO:8 or the complement thereof. Determining/comparing the percent identity of one nucleic acid sequence to another is "old hat" in the art, especially in view of the date in which the present application was filed.

The Examiner has asserted that "hybridization is only intended use of the nucleic acid which is not given any further patentable weight and does not alter or modify the claimed product." (see page 7 of the Office Action mailed on July 26, 2002). The applicants respectfully

submit that the Examiner is not clearly grasping the concept of "hybridization" as termed in the claims. Hybridization to a specific sequence, as claimed, correctly defines structural features that can only be common to the claimed genus. The specific sequence (in this case, SEQ ID NO:8 or SEQ ID NO:10) is the target in any hybridization technique that may be used to identify a binding partner (i.e. hybridization partner). One of ordinary skill in the art would readily agree that, in this specific case, no significant structural information can be obtained with regard to a sequence which *does not* hybridize to, for example, SEQ ID NO:8. Furthermore, one of ordinary skill in the art would readily agree that *definite* conclusions can be drawn with regard to structural features of a sequence that *does* bind to SEQ ID NO:8 as the sole target. Such features are, for example, the correct charge and spatial orientation of the hydrogen bond donors and acceptors that provide a specific binding surface for presentation to SEQ ID NO:8. The arrangement of donor and acceptor sites: 1) distinguish any binding sequence from non-binding sequences; 2) are an inherent feature of all nucleic acid sequences; and 3) readily allow one of ordinary skill in the art to make a determination as to whether or not the sequences harbor hydrogen bond donor and acceptor sites are in the "correct orientation" (i.e. if binding, then correct orientation; if no binding, then not in correct orientation). The three foregoing basic tenets define structure of nucleic acid segments. *It should be noted that all of these features are well known in the art, and were known well before the filing date of the present application.* Again, the art has established a strong correlation between nucleic acid structure and hybridization (i.e. function). One skilled in the art would be able to predict with a reasonable degree of confidence the structure of the claimed compositions from a recitation of

"hybridization" to SEQ ID NO:8 or SEQ ID NO:10. Whether or not the claimed nucleic acid segments harbor 80%, 90%, or 99% identity to SEQ ID NO:8, determinations as to structure are based upon whether or not the sequences hybridize to SEQ ID NO:8 under stringent conditions.

The foregoing discussion directly contradicts the Examiner's assertions that "no common elements or attributes of the sequences are disclosed and no structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided." Again, the common elements and attributes (i.e. structure) are defined by features (i.e. well known molecular forces at the interface between a nucleic acid and its target) that govern hybridization. Any one of ordinary skill in the art will attest that these features are inherent to all nucleic acid sequences. The question is whether, or not, these features are properly orientated to govern binding to the target nucleic acid, thereby defining structure. The method of isolation (hybridization) is predicated *on structure.*

Claims 1, 3-6, 9, and 11-14 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention.

The Examiner asserts that the pending claims expressly encompass genomic nucleic acids and not even complete cDNA sequences have been provided. It should be noted that the compositions (for example, claims 1, 4, 9, and 12) are directed to isolated or purified nucleic acid *segments* that hybridize to an isolated target sequence. One of ordinary skill in the art can

readily envision the detailed chemical structure of the claimed DNA sequences encoding for the proteins. The targets (i.e. SEQ ID NO:8 and SEQ ID NO:10) in combination with known hybridization methods provide one with the wherewithal to "see" the claimed structures.

The Examiner states that a "representative number", with regard to genus/species situations, depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. The number of claimed sequences are defined by the limits of hybridization as set forth in the claims. The target nucleic acids (SEQ ID NO:8 or SEQ ID NO:10) put a limit on the number, and types, of common attributes or features shared by the claimed members. Furthermore, the functional limitation, wherein the sequence encodes a 3-keto-acyl-CoA reductase protein, or a polyhydroxyalkanoate synthase protein, further defines the inherent features of the claimed compositions. Here, "hybridization" is limiting for both, functionality and structure, in view of the foregoing discussion. "Hybridization" *directly* impacts on the structure of nucleic acids. The target nucleic acid, which has *already been identified* (because it is a necessary hybridization reagent), is the "rate limiting" component in the hybridization assay. It is the "lock" that can only be accessed by the "key" (the nucleic acid exhibiting about 80% homology). **Nucleic acid *hybridization* extends beyond functional utility; it defines the chemical and structural makeup of the binding sequence.**

The Examiner has additionally asserted that there is no methodology presented to determine such common elements or attributes. In response, the applicants respectfully submit that, while the specification clearly discloses hybridization as the preferred method to determine

common structural features (i.e. define the claimed sequences), the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. *In re Bucher*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

In its Guidelines, the USPTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled *with a known or disclosed correlation between function and structure, or some combination of such characteristics.*" Guidelines, 66 Fed. Reg. at 1106 (emphasis added). Furthermore, in view of the well defined structural characteristics of nucleic acids (in general), the "functional" characteristics of nucleic acid/nucleic acid binding, and the fact that nucleic acid hybridization is well developed and mature, the applicants respectfully submit that the Examiner should find compliance with 35 U.S.C. § 112, first paragraph for claims directed to, for example, "an isolated or purified nucleic acid segment....that hybridizes to SEQ ID NO:8", notwithstanding the Examiner's asserted "functional" definition of the nucleic acids.

Allowance of claims 1, 3-6, 9, 11-14, 24 and 25 is respectfully solicited.

Respectfully submitted,

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Date: October 25, 2002

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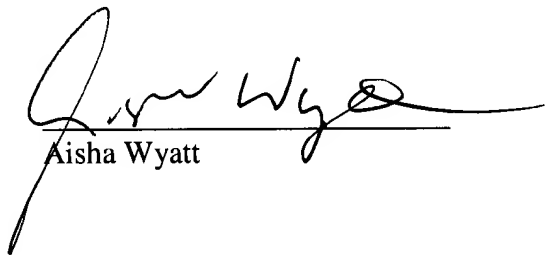

Aisha Wyatt

Date: October 25, 2002

Claims as Pending

1. (Three Times Amended) An isolated or purified nucleic acid segment comprising a nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein, wherein the nucleic acid sequence is a nucleic acid sequence at least about 80% identical to SEQ ID NO:8 that hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof, and

encodes a protein at least about 80% identical to SEQ ID NO:9, and

has 3-keto-acyl-CoA reductase activity higher for D-isomers of C6 carbon chains than for C4 carbon chains.

3. (Amended) A recombinant vector comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein;

b) a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein; wherein the structural nucleic acid sequence is a nucleic acid sequence at least about 80% identical to SEQ ID NO:8; that hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:9 and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains; and

c) a 3' transcription terminator.

4. (Amended) A recombinant cell comprising a nucleic acid segment encoding a 3-keto-acyl-CoA reductase protein, wherein the nucleic acid segment is a nucleic acid sequence at least

about 80% identical to SEQ ID NO:8; that hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:9 and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains.

5. (Amended) A genetically transformed plant cell comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein;

b) a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein; wherein the structural nucleic acid sequence is a nucleic acid sequence at least about 80% identical to SEQ ID NO:8 that hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:9 and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

6. (Amended) A genetically transformed plant comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein;

b) a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein; wherein the structural nucleic acid sequence is a nucleic acid sequence at least about 80%

identical to SEQ ID NO:8 that hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:9 and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

9. (Twice Amended) An isolated or purified nucleic acid segment comprising a nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein, wherein the nucleic acid segment is a nucleic acid sequence at least about 80% identical to SEQ ID NO:10 that hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:11 and that has polyhydroxyalkanoate synthase activity.

11. (Amended) A recombinant vector comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein;

b) a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein; wherein the structural nucleic acid sequence is a nucleic acid sequence at least about 80% identical to SEQ ID NO:10 that hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:11 and that has polyhydroxyalkanoate synthase activity; and

c) a 3' transcription terminator.

12. (Amended) A recombinant host cell comprising a nucleic acid segment encoding a polyhydroxyalkanoate synthase protein, wherein the nucleic acid segment is a nucleic acid sequence at least about 80% identical to SEQ ID NO:10 that hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:11 and that has polyhydroxyalkanoate synthase activity.

13. (Amended) A genetically transformed plant cell comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein;

b) a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein; wherein the structural nucleic acid sequence is a nucleic acid sequence at least about 80% identical to SEQ ID NO:10 that hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:11 and that has polyhydroxyalkanoate synthase activity;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

14. (Amended) A genetically transformed plant comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein;

b) a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein; wherein the structural nucleic acid sequence is a nucleic acid sequence at least about 80% identical to SEQ ID NO:10 that hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

encodes a protein at least about 80% identical to SEQ ID NO:11 and that has polyhydroxyalkanoate synthase activity;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

24. (Amended) The nucleic acid segment, vector, or cell of claims 1, 4, 5, or 6, wherein the nucleic acid sequence is SEQ ID NO:8.

25. The nucleic acid segment, vector or cell of claims 9, 11, 12, 13, or 14 wherein the nucleic acid sequence is SEQ ID NO:10.